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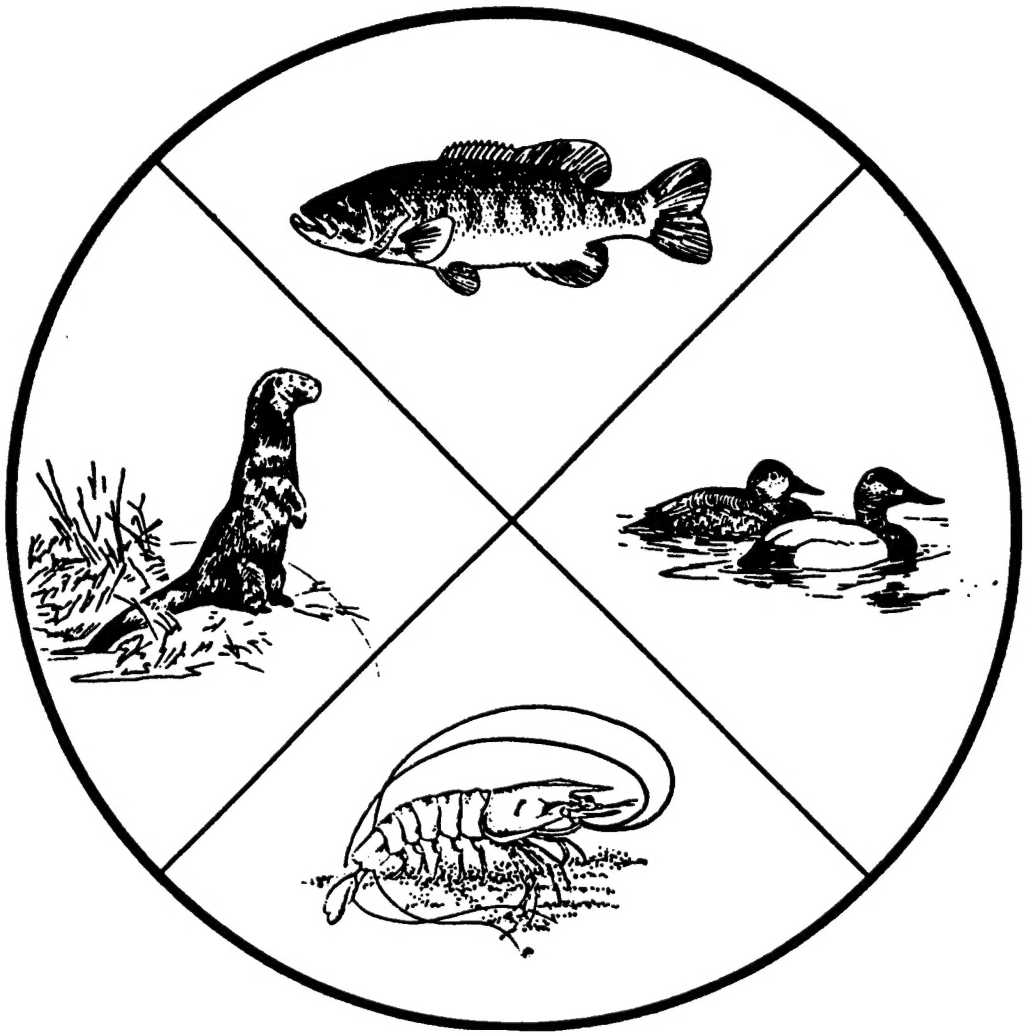
Contaminant Hazard Reviews
Report 28

Acrolein Hazards to Fish, Wildlife, and Invertebrates: A Synoptic Review



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By

Ronald Eisler

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Contents

	Page
Abstract	1
Sources and Uses	2
General	2
Sources	2
Uses	3
Environmental Chemistry	4
General	4
Chemical Properties	4
Persistence	5
Metabolism	6
Lethal and Sublethal Effects	7
General	7
Terrestrial Plants and Invertebrates	7
Aquatic Organisms	8
Birds	13
Mammals	15
Recommendations	25
Acknowledgments	27
Cited Literature	27

Tables

Number		Page
1	Chemical and other properties of acrolein	5
2	Acrolein effects on representative aquatic organisms.	9
3	Acrolein effects on birds.	14
4	Acrolein effects on selected mammals.	16
5	Proposed acrolein criteria for the protection of living resources and human health.	25

Acrolein Hazards to Fish, Wildlife, and Invertebrates: A Synoptic Review

by

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Abstract. Acrolein (CH_2=CHCHO) is the simplest member of the unsaturated aldehydes and enters the environment from incomplete combustion of fossil fuels, industrial discharges, herbicides, chemical control agents of fouling organisms, and normal metabolic processes of animals. Acrolein is volatile, flammable, and explosive. Biochemical and toxic effects of acrolein are caused by its reaction with sulfhydryl compounds to form a stable thiol ether. Acrolein metabolites under certain conditions are reportedly mutagenic, teratogenic, or carcinogenic. Acrolein degrades quickly in soils and in plant tissues; in water the half-time persistence is usually less than 50 h and in the atmosphere, less than 3 h. In treated irrigation canals, acrolein probably eliminates or seriously depletes all populations of aquatic fauna. Recommended herbicidal concentrations of acrolein for the control of submerged aquatic weeds usually exceed 1,000 µg/L; however, short-term tests with various species show that frog tadpoles die at 7 µg/L, representative fish are killed at 14 to 62 µg/L, and sensitive crustaceans are immobilized or die at 34 to 80 µg/L. Terrestrial plants and insects are comparatively resistant to acrolein; terrestrial plants tolerated 500 µg acrolein/L air and 25,000 µg/L in irrigation water, and adult fruitflies (*Drosophila melanogaster*), 3,700,000 µg acrolein/L culture medium. Birds are adversely affected by concentrations greater than 51 µg acrolein/kg whole egg by injection of eggs, greater than 9,100 µg/kg body weight (BW) by single oral doses, and greater than 50,000 µg/L (greater than 113 mg/m^3) by air concentrations. Mammals were affected by 50 µg acrolein/L air for 1 min, by 300 µg/L air for 10 min, and by intravenous injections of 850–6,000 µg/kg BW. Acrolein was fatal to mammals after exposure to 660 µg/L air for 24 days, 8,000–11,000 µg/L air for 4 h, 875,000 µg/L air for 1 min, and 4,000–28,000 µg/kg BW by single oral doses, or when fed diets equivalent to 500 µg/kg BW for 102 weeks. Proposed acrolein criteria for the protection of various resources include less than 15,000 µg/L in irrigation water of agricultural crops, less than 68 µg/L for aquatic fauna in acute exposures and less than 21 µg/L in chronic exposures, and less than 44 µg/L (less than 0.1 mg/m^3) in air for rats. No acrolein criteria are now available for the protection of avian and terrestrial wildlife. Acrolein criteria for the protection of human health include less than 320 µg/L in drinking water, less than 110 µg/L in air (less than 0.25 mg/m^3), and less than 0.68 µg/kg BW daily intake from all sources. More research is needed on acrolein and its metabolites.

Key words: Acrolein, aldehyde, herbicide, ecotoxicology, fish, aquatic plants, invertebrates, criteria.

Acrolein (CH_2=CHCHO) is an aldehyde that was first isolated in 1843 from the dry distillation of fats and glycerol (Beauchamp et al. 1985). It is now known that acrolein is ubiquitous in the environment; it is often present in trace amounts in foods and as a component of smog, fuel combustion products such as wood smoke, exhaust emissions from internal combustion engines, and cigarette smoke

(Smith 1962; U.S. Environmental Protection Agency [EPA] 1980; Beauchamp et al. 1985). Atmospheric concentrations of acrolein over urban areas are between 2 and 7 µg/L; cigarette smoke, however contains about 10,000 µg of acrolein/L (Beauchamp et al. 1985). Acrolein is classified as a hazardous chemical because of its reactivity and flammability (EPA 1980). At low sublethal concentrations, acrolein is widely known for its acrid pungent odor and strong irritating effects on mucous membranes of the eyes and of the upper respiratory tract, its toxicity to cilia in all organisms, and its interference with nucleic acid synthesis in bacteria (Marano and Puiseux-Dao 1982; Beauchamp et al. 1985). In bulk, acrolein during storage or transfer is potentially hazardous if it becomes overheated or contaminated with water. For example, in 1982, 17,000 residents from Toft, Louisiana, were evacuated when two large tanks of acrolein began to burn (Bowmer and Smith 1984).

Acrolein enters the aquatic environment from its use as an aquatic herbicide, from industrial discharges, and as a byproduct of the chlorination of organic compounds in wastewater and drinking water treatment (EPA 1980). Dilute solutions of acrolein kill undesirable plant life in irrigation streams and ditches (National Research Council [NRC] 1977) and have been used routinely in about 4,000 km of irrigation canals in southeastern Australia to control submerged weeds, including *Potamogeton tricarinatus*, *Elodea canadensis*, and *Vallisneria gigantia* (Bowmer and Smith 1984). Acrolein has also been used for many years in channel maintenance in the United States (especially in western states), Canada, Egypt, Argentina, Mexico, and Turkey (Bowmer and Smith 1984). Unlike most other aquatic herbicides, acrolein rapidly dissipates from the water by volatilization and degradation without leaving phytotoxic residues (Bowmer and Smith 1984; Parent et al. 1992). However, acrolein provides only temporary control of submerged weeds and also kills fish and other aquatic life at recommended treatment concentrations (Bowmer and Smith 1984). In one Montana stream, acrolein killed all fish in a 4-km stretch after application to control submerged weeds; some fish deaths were recorded as far as 6.4 km downstream (Fritz-Sheridan 1982). Useful reviews on ecological and toxicological aspects of acrolein are presented by Smith (1962), EPA (1980), Beauchamp et al. (1985), and the Agency for Toxic Substances and Disease Registry [ATSDR] (1990).

This report is part of a continuing series of brief reviews of environmental contaminants and their effects on living organisms with special emphasis on fishery and wildlife resources. It was prepared in response to requests for information on acrolein from environmental specialists of the U.S. Fish and Wildlife Service.

Sources and Uses

General

Acrolein enters the environment as a result of normal metabolic processes; incomplete combustion of coal, wood, plastics, tobacco, and oil fuels; and industrial emissions. Acrolein has been detected in smog, foods, and water. It is used extensively in chemical manufacture, for control of fouling organisms, and as an herbicide to control submerged weeds in irrigation canals.

Sources

Acrolein is ubiquitous in the environment as a result of natural and anthropogenic sources. Sources of atmospheric acrolein include smog; incomplete combustion of coal, wood, gasoline, plastics and fats; tobacco smoke; and industrial emissions. The total amount of acrolein released into the atmosphere is unknown. In 1978, production losses of acrolein by emission from the four main U.S. plant locations were estimated at 34,682 kg; however, the gaseous emission streams are now either burned on emergence from the exhaust stack or sent to a furnace to destroy residual material (Beauchamp et al. 1985). Acrolein is found in photochemical smog and contributes to the smog's irritant capacity to the eye and respiratory pathways (Beauchamp et al. 1985; Leikauf et al. 1989). Recorded maximum acrolein concentrations in smog ranged from 12 to 14 µg/L (0.025 to 0.032 mg/m^3) in Los Angeles between 1961 and 1963 and were 13 µg/L in Hudson County, New Jersey (EPA 1980). For humans, exposure to atmospheric acrolein is greatest in the vicinity of incompletely combusted organic materials such as coal, wood, and petrol; highest acrolein concentrations are reported near forest fires and urban area fires (Beauchamp et al. 1985; Srivastava et al. 1992). The burning of southern pine (*Pinus* sp.), for example, generates 22 to 121 mg of acrolein/kg of burned wood (EPA 1980). Acrolein is also in the smoke of burning plastic materials. Air samples from more than 200 fires in Boston, Massachusetts, contained greater than

3,000 µg acrolein/L (greater than 6.8 mg/m^3) in more than 10% of all samples; greater than 3,000 µg acrolein/L air is an immediately hazardous concentration for human life and health (Beauchamp et al. 1985). Cigarette smoke in some enclosed areas may account for as much as 12,400 µg of acrolein/L air (Feron et al. 1978; Astry and Jakab 1983; Beauchamp et al. 1985; Leikauf et al. 1989; Cohen et al. 1992). In the case of an enclosed room of 30 m^3 capacity, smoking 5 cigarettes raises the air concentration to about 50 µg acrolein/L and smoking 30 cigarettes, to 380 µg/L (EPA 1980).

Acrolein is also generated when animal or vegetable fats are subjected to high temperatures (Feron et al. 1978; EPA 1980). Acrolein was detected aboard submarines in trace concentrations as a degradation product during the heating of lubrication oils and edible fats (Lyon et al. 1970). Large amounts of acrolein are generated from exhausts of internal combustion engines (Astry and Jakab 1983; Heck et al. 1986; Ballantyne et al. 1989). Acrolein concentrations of 10,000 µg/L (23 mg/m^3) have been measured in nondiesel automobile exhausts, 2,900 µg/L in diesel engine emissions, and 2,600–9,600 µg/L in other internal combustion engines (EPA 1980). Acrolein concentrations in air from several urban areas in the United States ranged from a maximum of 10 µg/L in 1960 to 1.8–3.4 µg/L in 1968; air in Tokyo during this period had an average acrolein concentration of 7.2 µg/L (Beauchamp et al. 1985). Urban acrolein pollution is derived mainly from automobile exhaust and incomplete burning of refuse (Beauchamp et al. 1985). Acrolein is formed during normal metabolic degradation of spermine and spermidine, glycerol, allyl formate, allyl alcohol, and cyclophosphamide (EPA 1980; Marano and Puiseux-Dao 1982; Leach et al. 1987). Acrolein was also in spores from the wheat stem fungus (*Puccinia graminis*) of infected wheat (*Triticum aestivum*); acrolein was the major chemical factor that normally induced infection structure formation in *Puccinia* (Macko et al. 1978).

Acrolein has been detected in effluent-water streams from industrial and municipal sources. Municipal effluents from Dayton, Ohio, for example, contained between 20 and 200 µg acrolein/L in 6 of 11 analyzed samples (EPA 1980; Beauchamp et al. 1985). Acrolein is also a component of many foods, and processing may increase the acrolein content (EPA 1980). Acrolein has been identified in raw turkey, potatoes, onions, coffee grounds, raw cocoa beans, alcoholic beverages, hops (EPA 1980), white bread, sugarcane molasses, souring salted pork, and cooked bluefin tuna (*Thunnus thynnus*; Beauchamp et al. 1985).

Occupational exposure to acrolein may occur during its production and isolation as a chemical intermediate or during the manufacture of acrylic acid, acrylic acid esters, and methionine (Beauchamp et al. 1985). Other sources of acrolein in the workplace include emissions from rubber vulcanization plants, from welding of metals treated with anticorrosion primers, and from pitch-cooking plants and skin contact with herbicides during applications for aquatic weed control and with paper and paperboard, the manufacture of which includes acrolein as a slimicide. Acute acrolein poisoning from occupational exposure is improbable. However, the risks of poisoning are significant in certain industries including welding of fat and oil cauldrons, smelting work and foundry operations, printing plants, linoleum and oil cloth factories, manufacture of insulators, tin plating of sheet iron, and processing of linseed oil (Beauchamp et al. 1985).

Uses

Since its discovery in 1843, acrolein has been known to polymerize readily in the presence of many chemicals, and since 1947 it has been used safely in a wide variety of commercial applications (Albin 1962; Fischer 1962). Acrolein is presently produced by the catalytic oxidation of propylene for the manufacture of methionine, glutaraldehyde, 1,2,6-hexane thiol, and other chemicals. The largest quantity of acrolein produced by this process is converted directly to acrylic acid and acrylic acid esters (Beauchamp et al. 1985). In 1975, global production of acrolein was 59,000 metric tons; in 1980, this value was 102,000 tons—including 47,600 tons produced by the United States (EPA 1980). In 1983, about 250,000 tons (about 550 million pounds) of acrolein were produced; 92% was converted to acrylic acid and 5% to methionine; 3% was used as an aquatic herbicide (Beauchamp et al. 1985; Heck et al. 1986). Acrolein copolymers are used in photography, in textile treatment, in the paper industry, as builders in laundry and dishwater detergents, and as coatings for aluminum and steel panels (EPA 1980). Acrolein is used to scavenge sulfides from oil-field floodwater systems (Kissel et al. 1981), to crosslink protein collagen in the leather tanning industry, and to fixate tissue of histological samples (EPA 1980). The use of acrolein as a military poison gas has been advocated because

of its lacrimatory and blistering properties; during World War I the French used acrolein under the name of Papite in hand grenades because of its irritating effect on the respiratory airways and the ocular mucosa (Beauchamp et al. 1985).

Acrolein has been used since 1960 to control submerged aquatic weeds in irrigation systems in the United States, Australia, and other countries where open channels distribute water for crop production (Hill 1960; Bartley and Hattrup 1975; Bowmer and Higgins 1976; EPA 1980; Reinert and Rodgers 1987). Acrolein is preferable to sodium arsenite for herbicidal control of submerged weeds because arsenicals are persistent (as long as for 1 year) and the high arsenic concentrations that are attained in water may be hazardous to humans and livestock (Hill 1960). Acrolein is extremely effective in killing submerged weeds that are difficult to control with other herbicides (Hill 1960). Acrolein has also been used as an herbicide in ponds, drains, and other bodies of water (Donohue et al. 1966). In Australia, the concentration of acrolein in irrigation canals to control various species of *Elodea*, *Potamogeton*, and *Vallisneria* is usually less than 15,000 µg/L (Bowmer and Higgins 1976). In general, acrolein has a low order of toxicity to terrestrial plants (Donohue et al. 1966). Most field and garden crops can tolerate water with as much as 15,000 µg acrolein/L without serious adverse effects (Bartley and Hattrup 1975). Acrolein, as discussed later, has comparatively low persistence and low accumulation in aquatic ecosystems. One disadvantage to its use as an herbicide is its pungent, irritating odor (Hill 1960). At recommended treatment concentrations, however, acrolein kills fish and other aquatic organisms; therefore, acrolein should be used only in aquatic systems where these resources are considered expendable (Reinert and Rodgers 1987).

Acrolein has been used to control bacteria, fungi, algae, and molluscs in cooling-water systems: 1,500 µg/L killed as much as 95% of the target species in a once-through treatment (Donohue et al. 1966). Acrolein has been applied directly to the marine environment to control the growth and settlement of mussels (*Mytilus edulis*) and other fouling organisms in cooling-water systems of coastal steam-electric-station power plants (EPA 1980; Rijstenbil and van Galen 1981). Mussels in marine cooling-water systems are controlled with 600 µg acrolein/L for 8 h daily for 3 days or with 700 µg/L for 3 h daily for 2 weeks (Rijstenbil and van Galen 1981). Acrolein prevents the growth of microorganisms in liquid fuels such as jet fuels, in feed lines of subsurface wastewater injectors, and in water conduits of paper manufacturing plants (EPA 1980; Beauchamp et al. 1985).

Environmental Chemistry

General

Acrolein, the simplest member of the class of unsaturated aldehydes, has a pungent, irritating odor. It is volatile, flammable, and explosive and requires elaborate and specific conditions for storage and use. The half-time persistence of acrolein in freshwater is usually less than 50 h; in seawater it is less than 20 h and in the atmosphere less than 3 h. Biochemical and toxic effects of acrolein are caused by its rapid and essentially irreversible reaction with sulfhydryl compounds to form a stable thiol ether; however, many compounds can mitigate or block its toxicity. Acrolein is eventually metabolized to acrylic acid and glyceraldehyde; glycidaldehyde—an intermediate metabolite with mutagenic and carcinogenic properties—has been produced in vitro but not in vivo.

Chemical Properties

Acrolein is soluble in water and in many organic solvents including ethanol, acetone, and ether (Table 1; Beauchamp et al. 1985). Acrolein is a highly reactive molecule with two reactive centers: one at the carbon-carbon double bond and the other at the aldehydic group. Typical reactions involving acrolein are shown in detailed figures in Beauchamp et al. (1985). Acrolein is extremely volatile, flammable, and explosive (Table 1; Reinert and Rodgers 1987), especially in sunlight or in the presence of alkali or strong acid (Albin 1962; EPA 1980). A potential hazard in handling acrolein is its rapid exothermic polymerization caused by the use of insufficient hydroquinone inhibitor or lack of strict control of pH (Beauchamp et al. 1985). Commercial acrolein should be maintained at pH 6.0 and contain less than 3% water and 0.1–0.25% hydroquinone as a polymerization inhibitor. A typical commercial sample contains about 97% acrolein, 0.5% other carbonyls, and 2.5% water. The addition of hydroquinone (0.1–0.25%) prevents the vinyl polymerization of acrolein, and controlling the pH between 5 and 6 by acetic acid increases stability of commercial acrolein by preventing aldol condensation. Elaborate and specific conditions are now prescribed for the storage of

Table 1. Chemical and other properties of acrolein.[a]

Variable	Data
Chemical name	2-Propenal
Alternate names	Acraaldehyde, acraldehyde, acrolein, acryladehyde, acrylaldehyde, acrylic aldehyde, allyl aldehyde, aqualin, aquilin, Magnacide H, propenal
CAS Number	107-02-8
Structural formula	CH_2=CHCHO
Molecular weight	56.06
Specific gravity	0.8427–0.8442
Physical state	Colorless or yellow liquid at 25° C
Odor	Pungent, irritating
Boiling point	52.5–53.5° C
Melting point	–86.95° C
Solubility	
Water	206–208 g/L
Organic solvents	Miscible
Log K_{ow}	0.01
Vapor pressure	215–220 mm Hg at 20° C
Explosive limits of vapor and air	
Upper limit	31% acrolein
Lower limit	2.8% acrolein

[a] Hill (1960), Anderson and Hood (1962), Folmar (1977), EPA (1980), Hudson et al. (1984), Beauchamp et al. (1985), Mayer (1987), Reinert and Rodgers (1987), Ballantyne et al. (1989), Sine (1991), Agency for Toxic Substances and Disease Registry [ATSDR] (1990), National Institute for Safety and Health [NIOSH] (1990).

acrolein and include vents and safety valves, construction materials, fire control, spills, and waste disposal (Beauchamp et al. 1985). Commercial acrolein is stored and shipped under a blanket of oxygen-free inert gas (Albin 1962).

Spectrophotometric determination with 4-hexylresorcinol and a fluorometric method with m-aminophenol are the most commonly used procedures for the determination of acrolein; however, gas chromatography and high performance liquid chromatography procedures are also used (EPA 1980; Kissel et al. 1981; Nishikawa and Hayakawa 1986). Acrolein concentrations in rainwater between 4 and 200 µg/L can be measured rapidly (in less than 80 min) without interference from related compounds; the method involves acrolein bromination and analysis by gas chromatography with electron capture detection (Nishikawa and Hayakawa 1986). Kissel et al. (1981) emphasize that water samples from potential acrolein treatment systems require the use of water from that system in preparing blanks, controls, and standards and that acrolein measurements should be made at the anticipated use concentrations.

Persistence

Degradation and evaporation seem to be the major pathways for acrolein loss in water; smaller amounts are lost through absorption and uptake by aquatic organisms and sediments (EPA 1980; Reinert and Rodgers 1987). The half-time persistence of acrolein in freshwater is 38 h at pH 8.6 and 50 h at pH 6.6; degradation is more rapid when initial acrolein concentrations are less than 3,000 µg/L (Bowmer and Higgins 1976). At pH 5, acrolein reacts by reversible hydrolysis to produce an equilibrium mixture with 92% beta-hydroxypropionaldehyde and 8% acrolein; in alkali, the primary reaction is consistent with a polycondensation reaction (EPA 1980). In natural waters, acrolein degradation proceeds to carboxylic acid via a microbial pathway (EPA 1980); beta-hydropropionaldehyde is readily biotransformed in about 17.4 days (Reinert and Rodgers 1987).

Acrolein is applied to irrigation canals to control submerged aquatic weeds at greatly different time-concentration treatments. Regardless of time-concentration regimens—which vary from 100 µg/L for 48 h in the United States to 15,000 µg/L for several hours in Australia—the daily decay rate constants are remarkably similar, ranging from 0.14 to 0.21, and are probably affected by variations in weed density (O'Loughlin and Bowmer 1975; Parent et al. 1992). In one case, acrolein applied to the Columbia River at an average initial concentration of 125 µg/L degraded to 25 µg/L after 48 h in samples greater than 65 km from the application point—a loss of 80% (EPA 1980). High initial concentrations (50,000–160,000 µg/L) of acrolein in natural waters degraded 57 to 80% in 192 h, suggesting that high concentrations can alter the rate of hydrolysis (Kissel et al. 1981). In seawater, the half-time persistence of acrolein was less than 20 h (Rijstenbil and van Galen 1981). In photochemical smog, acrolein is comparatively unstable and not likely to persist; the dominant removal mechanism involves hydroxide attack on acrolein, and the atmospheric half-life persistence is 2–3 h under these conditions (Beauchamp et al. 1985).

Metabolism

Biochemical and toxic effects of acrolein are probably caused by its reaction with critical protein and nonprotein sulfhydryl groups (EPA 1980; Beauchamp et al. 1985; Heck et al. 1986). The reaction of acrolein with sulfhydryl compounds is rapid and essentially irreversible, resulting in the formation of a stable thiol ether (Beauchamp et al. 1985; Heck et al. 1986). Metabolism of acrolein is believed to result in the formation of acrylic acid and glyceraldehyde (Figure). The postulated metabolites of acrolein can be oxidized to carbon dioxide (Beauchamp et al. 1985). Acrylic acid does not seem to represent a significant toxic hazard when compared with the parent acrolein because at low airborne concentrations of less than 1,000 μg acrolein/L, the quantity of acrylic acid produced by metabolism is negligible. Thus, metabolism to acrylic acid after inhalation should be regarded as a detoxification pathway. Conjugation of acrylic acid with glutathione represents another elimination and detoxification pathway (Beauchamp et al. 1985). In-vitro studies of acrolein metabolism in mammals suggested that acrolein exposures may result in exposure to glycidaldehyde, an intermediate in acrolein metabolism (Figure). The major toxic effects of acrolein exposure—including irritation, ciliastasis, and hypersensitivity—are probably due either to the parent acrolein or to the reaction of glycidaldehyde with cell proteins. Glycidaldehyde is a potent mutagen and carcinogen; however, no evidence is available showing that acrolein can produce glycidaldehyde in vivo (Beauchamp et al. 1985). Acrolein is more toxic when inhaled than when taken orally (EPA 1980). Inhalation of acrolein decreased the concentrations of protein and nonprotein sulfhydryl groups in nasal mucosal tissue (Heck et al. 1986). Acrolein is highly reactive towards thiol groups and rapidly conjugates with glutathione and cysteine (EPA 1980). When glutathione is depleted, acrolein potentiates the nasal toxicity of formaldehyde to rats (Heck et al. 1986).

Acrolein is a metabolite of allyl alcohol and cyclophosphamide, and these compounds should be considered in acrolein metabolism schemes (Beauchamp et al. 1985; Cohen et al. 1992). Allyl alcohol in the presence of NADPH and liver or lung microsomes degrades to acrolein, acrylic acid, and glycidol (Figure).

When added to water as an aquatic herbicide, acrolein undergoes rapid decomposition, especially in the sunlight. At the same time, it reacts

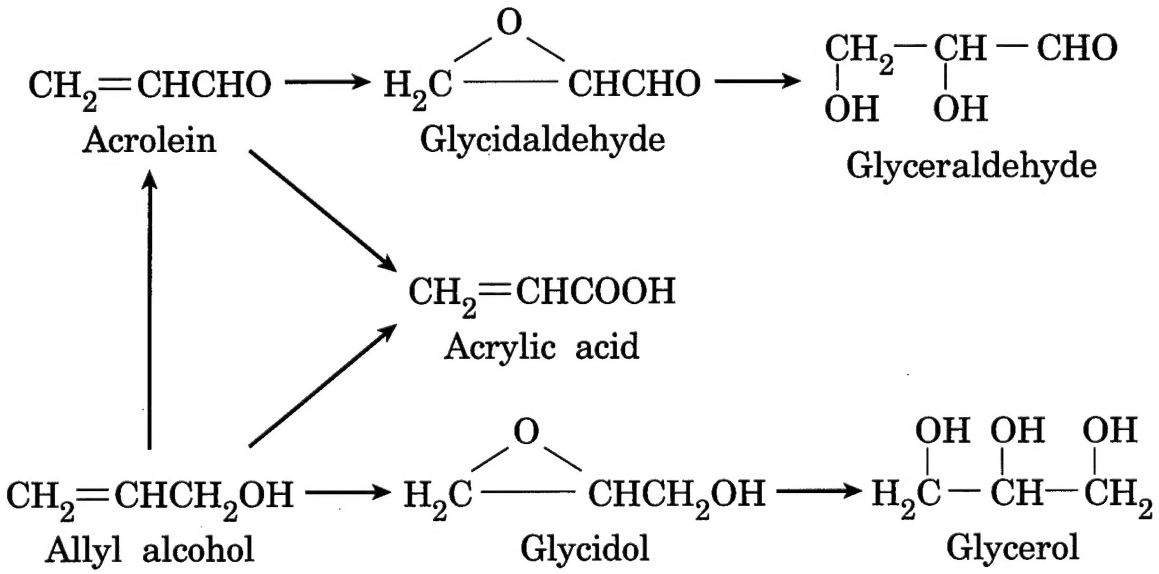

Figure. Proposed scheme for in vitro mammalian metabolism of acrolein and allyl alcohol, a precursor of acrolein (Beauchamp et al. 1985; ATSDR 1990).

rapidly with amines, alcohols, and mercaptans of aquatic plants, destroying cell structure and killing the plants (Parent et al. 1992). Mammals drinking acrolein-contaminated water rapidly convert acrolein to saturated alcohol compounds because of the low pH in the upper portion of their GI tracts; the primary breakdown product is beta-propionaldehyde (EPA 1980).

Many compounds including glutathione, 2-mercaptoethanol, beta-dimethylcysteamine, penicillamide, gamma-mercaptopropionylglycine, and N-acetylcysteine mitigate or block the toxic effects of acrolein (EPA 1980; Beauchamp et al. 1985; Heck et al. 1986). In frogs (*Rana japonica*), sulfhydryl compounds reduce the effects of acrolein on excitation-contraction uncoupling in skeletal muscle (Fujino et al. 1985). In mice, cysteine reduced the cytotoxic effects of acrolein on tumor cells; in rabbits, cysteine mitigated acrolein-induced alveolar macrophage calcium-dependent ATP-ase, phagocytosis, and adhesiveness (EPA 1980). In male rats, cysteine and ascorbic acid antagonized the acute lethal effects of orally-administered acrolein, and 2-mercaptoethanol antagonized the inhibitory effect of acrolein on liver DNA-polymerase (EPA 1980).

Lethal and Sublethal Effects

General

Acrolein degrades quickly in soils and in plant tissues regardless of mode of administration. Most terrestrial crop plants easily tolerate 25,000 µg of acrolein/L of irrigation water and some can tolerate 70,000–80,000 µg/L without adverse effects. Terrestrial plants were adversely affected at atmospheric concentrations of 500 µg acrolein/L air, but this concentration exceeds the recommended value of 110 µg/L (0.25 mg/m^3) air for protection of human health in occupational settings.

Adult fruitflies (*Drosophila melanogaster*) were comparatively resistant to acrolein and had lowered survival when reared in culture media with greater than 3,700,000 µg acrolein/L. At recommended concentrations for the control of nuisance submerged aquatic weeds (frequently 100–1,000 µg/L, often greater than 9,600 µg/L), acrolein was lethal or harmful to almost all aquatic vertebrates and invertebrates tested in short-term exposures. The most sensitive groups of tested aquatic organisms in short-term assays were frog tadpoles (dead at 7 µg/L) and representative species of fish (reduced survival at 14–62 µg/L) and crustaceans (death or immobilization at 34–80 µg/L). Adverse effects of acrolein on birds were observed at acute oral doses of 9,100 µg/kg BW (reduced survival), at concentrations greater than 51 µg/kg egg for egg injection (abnormal development and reduced survival), and at greater than 50,000 µg/L air (respiratory tract histopathology). In mammals, acrolein is a strong cytotoxic and ciliostatic agent that is irritating to mucous membranes of dermal, ocular, gastrointestinal, and respiratory systems and is systemically toxic by all routes of exposure. Adverse effects of acrolein are documented in sensitive species of mammals under the following regimens: 50 µg/L air for 1 min (increased blood pressure and heart rate); 300 µg/L air for 10 min (ocular and nasal irritation); 500 to 1,000 µg/L air (repelled by odor); 660 µg/L air for 24 days (reduced survival); 8,000 to 11,000 µg/L air for 4–6 h or 875,000 µg/L air for 1 min (death); dietary concentrations equivalent to 500 µg/kg BW for 102 weeks (decreased survival); 850–6,000 µg/kg BW by intravenous injection (liver necrosis, embryo resorption); and single oral doses between 4,000 and 28,000 µg/kg BW (death).

Acrolein was mutagenic to certain microorganisms and to the fruitfly; mutagenicity may be due, in part, to glycidaldehyde, an acrolein metabolite. Injected into the amniotic fluid, acrolein is teratogenic to rats; teratogenicity may be due to acrylic acid, an acrolein metabolite. There is limited evidence that acrolein acts as a weak carcinogen and tumor promoter. Acrolein interacts with other chemicals, sometimes synergistically, additively, or antagonistically. Also, some chemicals normally contain acrolein as an impurity or yield acrolein as a metabolite.

Terrestrial Plants and Invertebrates

Most crop plants easily tolerate irrigation water with 25,000 µg of acrolein/L and many tolerate 70,000 to 80,000 µg/L without adverse effects—including corn (*Zea mays*), cotton (*Gossypium hirsutum*), milo (*Sorghum* spp.), squash (*Cucurbita* spp.), castor bean (*Ricinus communis*), tomato (*Lycopersicon esculentum*), alfalfa (*Medicago sativa*), and sugarcane (*Saccharum officinarum*; Ferguson et al. 1961). Acrolein degrades quickly in soils and plant tissues regardless of mode of administration (Ferguson et al. 1961). Atmospheric concentrations of 500 µg acrolein/L and higher were harmful to certain plants (Beauchamp et al. 1985). Leaves of

the pinto bean (*Phaseolus* spp.) and the morning glory (*Ipomoea* spp.) developed brown foliar lesions after exposure to 500 µg/L air for 4–7 h; damage was more severe if the plants were moist during exposure. Leaves of the radish (*Raphanus* spp.) developed lesions after exposure to 1,500 µg acrolein/L air for 6–7 h; however, leaves of the geranium (*Geranium* spp.) and the tomato showed no adverse effects after exposure to 1,500 µg/L air for 7 h (Beauchamp et al. 1985).

Acrolein inhibits DNA, RNA, and protein synthesis in the bacterium *Escherichia coli*, and this inhibition probably accounts for its cytotoxic and inhibitory effects on *E. coli* cell division (EPA 1980; Beauchamp et al. 1985). Acrolein is demonstrably mutagenic to microorganisms and to larvae of the fruitfly (*Drosophila melanogaster*). Acrolein-induced mutagenicity—including point mutations, sister chromatid exchanges, and chromosome breakages—has been observed in selected strains of bacteria (*E. coli*, *Salmonella typhimurium*), yeast (*Saccharomcyces cerevisiae*), fruitfly larvae, and cultured Chinese hamster ovary cells (EPA 1980; Beauchamp et al. 1985; Sierra et al. 1991; Cohen et al. 1992). Acrolein's mutagenicity may be due to the metabolite glycidaldehyde; glycidaldehyde was mutagenic to bacteria and yeast under controlled conditions (Beauchamp et al. 1985; Sierra et al. 1991). Studies with *D. melanogaster* show that acrolein is mutagenic in the sex-linked recessive lethal test when injected but not when fed (Sierra et al. 1991). Acrolein caused 2.2% sex-linked mutations in *D. melanogaster*—the highest percentage recorded among several tested aldehydes (EPA 1980). In studies by Comendador (1984), early embryonic stages of fruitflies were most sensitive to the mutagenic properties of acrolein and sensitivity decreased with increasing development to the point that adults showed negligible mutagenic responses. Adults of the fruitfly were generally resistant to acrolein; mortality was 25% when the culture medium contained 3,700,000 µg of acrolein/L, 50% at 8,600,000 µg/L, and 75% at 22,100,000 µg/L (Comendador 1984).

Aquatic Organisms

Adverse effects of acrolein on sensitive groups of aquatic organisms are documented (Table 2) at concentrations—in µg acrolein/L medium—as low as 7 for frog tadpoles (death), 14–62 for fish (death), 34–80 for crustaceans (death, immobilization), 50 for oysters (reduction in shell growth rate), 100–200 for freshwater algae (DNA and RNA reduction, photosynthesis inhibition), 151 for gastropods (death), >151 for insects (death), 500–2,000 for macrophytes (leaf cell deterioration, death), 1,250 for trematodes (death of miracidia in 20 min), and 62,000 for bacteria (growth reduction). Aquatic vertebrates were more sensitive than invertebrates (Holcombe et al. 1987), and younger fish were more sensitive than older fish (Burdick et al. 1964). Aquatic insects do not avoid acrolein at concentrations that repel fish (Folmar 1978).

As an herbicide, acrolein is most effective in controlling dense accumulations of submerged weeds in habitats where waterflow is rapid and uniform, such as irrigation canals and rapidly-flowing streams (Ferguson et al. 1961). Acrolein is lethal to various genera of submerged plants (*Hydrodictyon*, *Spirogyra*, *Potamogeton*, *Zannichellia*, *Cladophora*, *Ceratophyllum*, *Elodea*, *Chara*, *Najas*) at 1,500 to 7,500 µg/L (Ferguson et al. 1961; Beauchamp et al. 1985). But some floating plants (*Pistia*, *Eichornia*, *Jussiaea*) are more resistant to acrolein than submerged plants and require concentrations that are at least double those necessary for submerged forms (Ferguson et al. 1961). Acrolein has little effect on emergent aquatic macrophytes and should not be used to control emergents (Ferguson et al. 1961). In Australia, acrolein is the only herbicide now used for control of submerged aquatic weeds in larger irrigation canals (Bowmer et al. 1979); effective plant control was obtained at 9.6–28.8 mg/L for 3 h (Bowmer and Smith 1984). In the United States, the U.S. Bureau of Reclamation controls aquatic algae and weeds at lower concentrations (0.1 mg/L) and longer exposures (48 h; Folmar 1980). In the Columbia River basin in the state of Washington, acrolein is used to control submerged aquatic macrophytes at concentrations of 0.1 mg/L for 48 h or 1.0 mg/L for 4 to 8 h with applications every 3 to 5 weeks (Bartley and Hattrup 1975). Vegetation destruction by acrolein is maximal 1 week after application, and green filmenentous algae are usually the first plants to return after 1 month (Ferguson et al. 1961). Biomass and species diversity were altered in acrolein-treated phytoplankton populations in Egyptian irrigation canals 1 year after treatment (Kobbia 1982). Although acrolein is a powerful cytotoxic agent, its inhibitory effects at sublethal concentrations on plant mitosis, nucleic acid synthesis, and protein synthesis are considered completely reversible (Marano and Puiseux-Dao 1982).

Table 2. Acrolein effects on representative aquatic organisms.

Taxonomic group, organism, concentration, and other variables	Effect	Reference[a]
Bacteria, Algae, and Macrophytes		
Fresh water algae, *Anabaena* sp.; 690 µg/L; 24-h exposure	50% reduction in photosynthesis at 25° C	1
Aquatic bacteria, 3 species		
62,000 µg/L; 48-h exposure	Some growth reduction, but recovery by 120 h	2
125,000 µg/L; 120-h exposure	LC100	2
500,000 µg/L; 2-h exposure	LC100	2
Freshwater alga, *Cladophora glomerata*		
100 µg/L	Onset of photosynthesis inhibition at 30° C	1
760 µg/L; 24-h exposure	50% reduction in photosynthesis at 30° C	1
1,000 µg/L; 24-h exposure	50% reduction in photosynthesis at 25° C	1
Alga, *Dunaliella bioculata*		
100 µg/L; 48-h exposure	DNA concentration reduced 28%	3
200 µg/L; 48-h exposure	DNA concentration reduced 36% and RNA 28%	3
400 µg/L; 48-h exposure	DNA reduced 93%, RNA 68%, and proteins 74%	3
1,000 µg/L; 48-h exposure	No development in 48 h	3
8,000 µg/L; 3-h exposure	Ultrastructural anomalies, and cytoplamic inclusions	4
Elodea, *Elodea canadensis*		
Sublethal (actual exposure concentration and duration unknown)	Growth stimulation (from reduced competition by aufwuchs, bacteria, and epiphytic algae)	5
500 µg/L; 24-h exposure	Leaf cell deterioration	6,7
2,800 µg/L; 3-h exposure in irrigation canal	80% reduction in density; recovery began in 17 days	5
15,000 µg/L; 2–6 h exposure in Australian canals	Effective control for up to 21 km in flowing-water irrigation canals	8
18,000 µg/l; 2 to 12 h exposure in smaller channels and up to 72 h in major canals; New South Wales	Effective control	5
22,000 µg/L; 3-h exposure in irrigation canal	94% reduction in biomass after 14 days	5
Filamentous algae, unidentified		
500 µg/L; 5-months exposure; petroleum-refinery recirculating cooling-water system	Effective control	9
1,000 µg/L; 20-h exposure in Arizona irrigation canal	Effective control for 2 weeks	10
3,500 µg/L; 2-weeks exposure in petroleum refinery cooling water	Lethal	9
5,000 µg/L; 1-week exposure in petroleum refinery cooling water	Lethal	9

Table 2. *Continued.*

Taxonomic group, organism, concentration, and other variables	Effect	Reference[a]
Freshwater alga, *Enteromorpha intestinalis*		
1,800 µg/L; 24-h exposure	50% reduction in photosynthesis at 25° C	1
2,500 µg/L for 24 h	50% reduction in photosynthesis at 20° C	1
>5,000 µg/L for 24 h	50% reduction in photosynthesis at 15° C	1
Freshwater plants; 6 species of submerged plants, 2 species of floating plants, 4 groups of phytoplankton; irrigation drains, Egypt; 15,000–25,000 µg/L for 45 min, repeated 4 times;	Effective control of all plants within 2–7 days. Phytoplankton recovery over 1-year period was most rapid for the Cyanophycae, followed by the Bacilliarophyceae, Chlorophycae, and Euglenophyceae, and resulting in altered biodiversity when compared with a control canal	11
Submerged macrophytes, 3 species (*Najas* sp., *Ceratophyllum* sp., and *Ipomoea* sp.); 25,000 µg/L	All dead 1 week after application	6
Floating pondweed, *Potamogeton carinatus*		
2,000 µg/L for 12 h	LC50	12
10,000–15,000 µg/L for >1 h (actual exposure time unknown)	LC50	12
15,000 µg/L for 1.7 h	LC50	12
22,000–26,000 µg/L for >1 h (actual exposure time unknown)	LC80	12
Pondweed, *Potamogeton crispus*; 20,000 µg/L for 5 h	All dead in 8 days	6
Pondweed, *Potamogeton tricarinatus;* 4,000 µg/L; 1-h exposure in irrigation canal	Minimum effective concentration	5
Submerged macrophyte, *Vallisneria gigantea*; 26,000 µg/L for 1 h in irrigation canal	Minimum effective concentration	5
Ribbonweed, *Vallisneria spiralis*		
1,600 (95% confidence interval [CI] of 1,300–2,000) µg/L	50% reduction in biomass	12
3,700 (95% CI of 3,200–4,600) µg/L for 1 h	80% reduction in biomass	12
Invertebrates		
Snail, *Aplexa hypnorum*; 151 µg/L for 96 h	Less than 50% mortality	13
Snail, *Australorbis glabratus*		
1,250 µg/L for 24 h	All adults and 90% of embryos survived	7
2,500 µg/L for 24 h	35% of adults and 40% of embryos died	7
10,000 µg/L for 24 h	98% of adults and 100% of embryos died	6,7
Barnacle, *Balanus ebarneus*; 1,600–2,100 µg/L for 48 h	LC50	6
American oyster, *Crassostrea virginica*; 50–55 µg/L for 96 h	50% reduction in shell growth rate	6, 14, 15

Table 2. *Continued.*

Taxonomic group, organism, concentration, and other variables	Effect	Reference[a]
Daphnid, *Daphnia magna*		
17–34 µg/L	MATC[b]	6, 16
51 (95% CI of 43 to 62) µg/L for 48 h	50% immobilized	13
57–80 µg/L for 48 h	LC50	6
Mayfly, *Ephemerella walkeri*; 100 µg/L for 1 h	No avoidance of acrolein by nymphs	17
Freshwater snails, 3 species (*Physa, Biomphalaria, Bulinus*); 25,000 µg/L for 3.5–4 h	All dead	14
Common mussel, *Mytilus edulis*		
200–1,000 µg/L; exposed for as much as 8 h daily for 3 days	Valves closed immediately after start of exposure to acrolein regardless of concentration or duration; effect in 45% of mussels at 200 µg/L, 80% at 400 µg/L, and 90% at 600 µg/L	8
600 µg/L; single 8-h exposure followed by 48-h of uncontaminated seawater	70% of the mussels (1–2.5 mm shell length) in the cooling water systems of power plants became detached in 3 days vs.13% of controls	18
600 µg/L; 8-h exposure daily for 3 days	97% of mussels became detached	18
600 µg/L; 29-h continuous exposure	100% detachment	18
Brown shrimp, *Penaeus aztecus*		
100 µg/L for 48 h	LC50	14
100 µg/L for 48 h	50% loss in equilibrium	6, 15
Trematode, *Schistosoma mansoni*		
1,250 µg/L for 20 min	Killed all miracidia	7
2,500 µg/L	Killed all miracidia in 10 min, and all cercariae in 18 min	7
Midge, *Tanytarsus dissimilis*; 151 µg/L for 48 h	Less than 50% mortality	13
Vertebrates		
Bowfin, *Amia calva*; 62 µg/L for 24 h	LC50, fry	14
Goldfish, *Carassius auratus*		
80 µg/L for 24 h	LC50	6
1,000–2,000 µg/L for 3 h	Fatal	14
White sucker, *Catostomus commersoni*; 14 (95% CI of 8–25) µg/L for 96 h	LC50	13
Longnose killifish, *Fundulus similis*; 240 µg/L for 48 h	LC50	6,15
Western mosquitofish, *Gambusia affinis*		
61 µg/L for 48 h	LC50	6, 14
149 µg/L for 24 h	LC50	14

Table 2. *Continued.*

Taxonomic group, organism, concentration, and other variables	Effect	Reference[a]
Bluegill, *Lepomis macrochirus*		
13 µg/L for 28 days	Whole fish, bioconcentration factor of 344	6
33 (95% CI of 27–40) µg/L for 96 h	LC5	13
79 µg/L for 24 h	LC50	6, 19
90–100 µg/L for 96 h	LC50	6, 14
Largemouth bass, *Micropterus salmoides*		
160 µg/L for 96 h	LC50	6, 14
183 µg/L for 24 h	LC50	14
Rainbow trout, *Oncorhynchus mykiss*		
8 µg/L for 48 h	None dead	20
16 (95% CI of 14–19) µg/L for 96 h	LC50	13
20, 50, or 100 µg/L; exposure for 4 h; trout collected 1, 4, and 7 days postexposure; cooked fillets evaluated for odor and taste by human panel	Unacceptable organoleptic qualities were recorded for fillets 1 and 4 days (P = 0.05) after treatment with 100 µg/L; some unacceptable qualities were detected 1 and 4 days after treatment with 50 µg/L, and at 7 days after treatment with 100 µg/L	17
29 (95% CI of 22–37) µg/L for 96 h	LC50	21
48 µg/L for 48 h	LC32	6, 20
65 µg/L for 24 h	LC50, fingerlings	6
77 µg/L for 20.5 h	LC50	21
90 µg/L for 4.8 h	No deaths	20
96 µg/L for 48 h	All dead	20
100 µg/L for 1 h	Avoidance by fry	6, 14, 23
150 µg/L	Lethal	22
240 µg/L for 4.8 h	LC10	20
410 µg/L for 4.8 h	LC70	20
>500 µg/L for 4.8 h	All dead	20
Chinook salmon, *Oncorhynchus tshawytscha*; 80 µg/L for 24 h	LC50	6, 19
Fathead minnow, *Pimephales promelas*		
11.4–41.7 µg/L	MATC[b]	6, 16
14 (95% CI of 8–25) µg/L for 96 h	LC50	13
84 µg/L for 6 days	LC50	6
115 µg/L for 48 h	LC50	6, 14
150 µg/L for 24 h	LC50	14
Harlequin fish, *Rasbora heteromorpha;* 130 µg/L for 48 h	LC50	14
Brown trout, *Salmo trutta*		
46 µg/L for 24 h	LC50	6, 14, 19
1,500 µg/L for 76–138 min	All dead	19
6,000 µg/l for 28–61 min	All dead	19
16,000 µg/L for 15–39 min	All dead	19
Frog, *Xenopus laevis*, tadpoles; 7 (95% CI of 6–8) µg/L for 96 h	LC50	13

[a] 1, Fritz-Sheridan 1982; 2, Starzecka 1975; 3, Marano and Puiseux-Dao 1982; 4, Baron-Marano and Izard 1968; 5, Bowmer and Smith 1984; 6, EPA 1980; 7, Ferguson et al. 1961; 8, Bowmer et al. 1979; 9, Donohue et al. 1966; 10, Corbus 1982; 11, Kobbia 1982; 12, Bowmer and Sainty 1977; 13, Holcombe et al. 1987; 14, Folmar 1977; 15, Mayer 1987; 16, Beauchamp et al. 1985; 17, Folmar 1978; 18; Rijstenbil and van Galen 1981; 19, Burdick et al. 1964; 20, Bartley and Hattrup 1975; 21; McKim et al. 1987; 22, Kissel et al. 1981; 23, Folmar 1976.

[b] Maximum acceptable toxicant concentration. Lower value in each pair indicates highest concentration tested producing no measurable effect on growth, survival, reproduction, or metabolism during chronic exposure; higher value indicates lowest concentration tested producing a measurable effect.

Acrolein in concentrations sufficient to control nuisance submerged aquatic weeds may also kill snails, crayfish, shrimp, fish, and toads (Ferguson et al. 1961). In one case, acrolein was used to control *Potamogeton* and *Chara* in an Ohio farm pond during June 1960 (Hill 1960). Acrolein was applied at 16,100 µg/L to a 0.1 ha portion of the 0.7 ha pond. Within 1 h of application, many dead amphibian tadpoles and small bluegills (*Lepomis macrochirus*) were recovered. In 24 h, *Chara* had turned white and *Potamogeton* brown; both plant species seemed dead; fish were swimming in the treated area. In 72–96 h, several large dead walleyes (*Stizostedium vitreum vitreum*) were found. One week posttreatment, all algae and weeds in the treated area were dead; weeds were present in the untreated areas. The treated section remained weed-free for 4–6 weeks; after 8 weeks, the treated area was heavily infested with *Chara*. Hill (1960) concluded that tadpoles, walleyes, and small bluegills were more susceptible to acrolein toxicity than larger bluegills and bass (*Micropterus* spp.) in the pond. Acrolein is also effective in controlling trematodes that cause schistosomiasis wherein snails are the intermediate host, especially in irrigation systems. For example, native species of snails (*Lymnaea, Helisoma*), along with *Potamogeton* weeds, were destroyed within 12 km in the main irrigation canal of Kern County, California, after a single application of acrolein (Ferguson et al. 1961).

Acrolein was the most toxic of 15 herbicides tested for toxicity to fish (EPA 1980). Responses by rainbow trout (*Oncorhynchus mykiss*) surviving 77 µg acrolein/L, a concentration that killed 50% in about 21 h, were characteristic of respiratory irritants (McKim et al. 1987). These responses included a steady increase in cough rate; decreases in ventilation rate, oxygen utilization, and heart rate; increases in hematocrit; and decreases in total arterial oxygen, carbon dioxide, and pH (McKim et al. 1987). In studies by Bartley and Hattrup (1975), no-observable-effect concentrations of acrolein for rainbow trout were 240 µg/L for exposures of 4.8 h and 48 µg/L for exposures of 48 h; these values are below the concentrations that control aquatic weeds. In the same study, rainbow trout that survived exposure to high sublethal concentrations for 48 h were unable to recover completely after acrolein treatments were ended. Trout and other teleosts are poorly adapted to detoxify acrolein and other xenobiotic aldehydes (Parker et al. 1990). The low metabolic capacity of fish liver aldehyde dehydrogenase for aldehydes, in general, suggests that these compounds may be hazardous to fish populations (Parker et al. 1990). Applications of acrolein to waters where fish may be taken for human consumption should be made with caution; rainbow trout surviving exposure to acrolein in reservoirs or connecting canals frequently presented odor and taste problems to human consumers (Folmar 1980).

Acrolein is used also to control fouling organisms in cooling water systems. Effective control was established in a once-through cooling system of a steel mill with continuous application of 200 µg acrolein/L (Donohue et al. 1966). Acrolein controlled bacteria in condenser pipes of a powerplant cooling system but only at extremely high concentrations of 125,000 µg/L for 120 h or 500,000 µg/L for 2 h (Starzecka 1975). Acrolein reduced settlement of young mussels (*Mytilis* sp.) in cooling seawater systems of power plants (Rijstenbil and van Galen 1981). In recirculating cooling water systems, algae and bacteria can be controlled at 500 µg/L for 5 months or at 5,000 µg/L for 1 week (Table 2).

Birds

Acrolein was lethal to birds at single oral doses of 9,100 µg/kg BW (Table 3). Observed signs of acrolein poisoning in subadult mallards (*Anas platyrhynchos*) after oral administration included regurgitation, a reluctance to leave the swimming area, slow responses, muscular incoordination, heavy-footed walking, phonation, wing tremors, running and falling, weakness, and withdrawal (Hudson et al. 1984). Treatment concentrations as low as 3,300 µg/kg BW have produced signs of acrolein poisoning. These signs appeared as soon as 10 min after administration and persisted for as long as 36 days. At lethal oral concentrations, deaths occurred as soon as 32 min posttreatment and continued for several days (Hudson et al. 1984). Acrolein was lethal to developing avian embryos when whole eggs were injected with 51 to 182 µg/kg FW; in descending order, embryos were most sensitive when acrolein was administered by way of the yolk sac (51 µg/kg), by the inner shell (82 µg/kg), and by the air sac (182 µg/kg; Table 3). Acrolein is 50 times more toxic to embryos of the domestic chicken (*Gallus* sp.) than acrylonitrile and 100 times more toxic than acrylamide (Kankaanpaa et al. 1979). Acrolein inhibits mucous transport in the trachea of the domes-

Table 3. Acrolein effects on birds.

Organism, route of administration, dose, and other variables	Effect	Reference[a]
Mallard, *Anas platyrhynchos*; oral route; 9,100 µg/kg body weight (BW), 95% confidence interval [CI] of 6,300–13,100 µg/kg BW	LD50, age 3–5 months	1
Domestic chicken, *Gallus* sp.		
Inhalation route		
Adults subjected to 50,000 or 200,000 µg acrolein/L (113 or 454 mg/m^3) air via an endotracheal cannula for up to 27 days	Decreases in trachea complement of ciliated and goblet cells; inhibited mucoous transport activity in trachea; lymphocytic inflammatory lesions in the tracheal mucosa. Changes were more pronounced at the higher dose and with increasing exposures	2
Air sac injection route. Embryos 2–3 days old; examined at day 13		
>127 µg/kg fresh weight (FW) whole egg	Dose-dependent decrease in survival	3
182 µg/kg FW whole egg	LD50	3
1,818 µg/kg FW whole egg	LD80	3
Air sac injection route. Embryos, 3-days old		
1 µg/kg FW whole egg	20% developmental abnormalities vs. 5% in controls	4
10 µg/kg FW whole egg	No malformations	4
1,000 µg/kg FW whole egg	Lethal	4
Inner shell injection of membrane on heart route. Embryos, 72–76 h old; examined on day 14 of incubation		
25 µg/kg FW whole egg	No deaths or malformations	5
51 µg/kg FW whole egg	50% dead or malformed	5
82 µg/kg FW whole egg	LD50	5
102 µg/kg FW whole egg	71% dead, 6% malformed	5
203 µg/kg FW whole egg	97% dead, 3% malformed	5
Yolk-sac injection route. Embryos 3-days old, examined at day 14		
51 µg/kg FW whole egg	LD50	6
1,018 µg/kg FW whole egg	LD90; no evidence of increased teratogenicity over controls	6

[a] 1, Hudson et al. 1984; 2, Denine et al. 1971; 3, Chhibber and Gilani 1986; 4, Beauchamp et al. 1985; 5, Korhonen et al. 1983; 6, Kankaanpaa et al. 1979.

tic chicken (Denine et al. 1971), probably through ciliostatic action (EPA 1980). Adverse effects of acrolein were observed on chicken respiratory-tract physiology and pathology at greater than 50,000 µg/L air (Table 3).

Malformations of the eye, coelom, neck, back, wings, and legs were observed in surviving acrolein-treated chicken embryos (Korhonen et al. 1983) after whole eggs were injected with greater than 51 µg acrolein/kg FW (Table 3). In other studies, acrolein showed no clear evidence of teratogenicity in chicken embryos, although there is a dose-dependent embryotoxic effect (Beauchamp et al. 1985; Chhibber and Gilani

1986). Acrolein-treated chicken embryos had a higher frequency of abnormal limbs, abnormal neck, and everted viscera than the controls, but the frequency was not dose-related. The overall incidence of abnormal embryos when treated at age 48 h was 24% but only 4% in controls; in embryos given acrolein at age 72 h, these values were 26% and 12% in controls (Chhibber and Gilani 1986).

Mammals

Acrolein is a strong cytotoxic and ciliostatic agent; its irritating effects on mucous membranes and its acute inhalation toxicity in mammals are well documented (Feron and Kruysse 1977; Feron et al. 1978; EPA 1980; Astry and Jakab 1983; Beauchamp et al. 1985; Leach et al. 1987; Leikauf et al. 1989). A characteristic of acrolein is its pungent, offensive, and acrid smell that is highly irritating to ocular and upper respiratory-tract mucosae (Beauchamp et al. 1985). Acrolein is toxic by all routes of exposure, and many of its toxic and biochemical effects are produced by interfering with critical sulfhydryl groups (Srivastava et al. 1992). In isolated rat-liver fractions, acrolein is a potent inhibitor of the high-affinity aldehyde dehydrogenase isozymes in mitochondrial and cytosolic fractions (Mitchell and Petersen 1988). Acrolein impairs DNA replication in vitro and inhibits certain mitochondiral functions (Feron et al. 1978). Studies with isolated rat liver-membrane proteins revealed that acrolein inhibits plasma membrane enzymes and alters the membrane protein profile; this may be due to acrolein-induced polymerization of plasma-membrane proteins (Srivastava et al. 1992).

Measurable adverse effects of acrolein have been documented in representative species of mammals, but the severity of the effects are contingent on the mode of administration, concentration, dose, and duration of exposure (Table 4). Single oral doses of 4,000 µg/kg BW were lethal to guinea pigs and 28,000 µg/kg BW to mice; diets containing the equivalent of 500 µg/kg BW and more decreased survival in rats after 102 weeks (Table 4). Concentrations of 60,000 µg acrolein/L in drinking water had no measurable adverse effects on cows (*Bos* sp.) after 24 h; rats initially rejected drinking water containing 200,000 µg/L but eventually tolerated this concentration (Table 4). Dermal toxicity seems low; rabbits that were immersed up to their necks in water containing 20,000 µg acrolein/L for 60 min showed no adverse effects (Table 4). No dermal sensitization occurred in healthy female guinea pigs (*Cavia* spp.) after repeated skin exposures to acrolein (Susten and Breitenstein 1990). In undiluted liquid or pungent vapor form, however, acrolein produces intense irritation of the eye and mucous membranes of the respiratory tract, and direct contact with the liquid can produce skin or eye necrosis (Beauchamp et al. 1985). A single intravenous injection of 850 µg acrolein/kg BW produced liver necrosis in rats; 6,000 µg/kg BW caused increased embryo resorption in mice (Table 4). Rats receiving near-lethal doses of acrolein by subcutaneous injection had liver and kidney damage and lung pathology (EPA 1980). Although subcutaneous injections revealed LD50 values between 164,000 and 1,022,000 µg/kg BW in rabbits, these results are questionable because acrolein may be sequestered at the injection site and delay delivery to the systemic circulation (Beauchamp et al. 1985). A single intraperitoneal injection of 1,000 µg/kg BW caused peritonitis in rats, and 7,000 µg/kg BW was lethal to mice; daily injections of 1,000 µg/kg BW were eventually lethal to rats (Table 4). Sublethal intraperitoneal injections of acrolein induced ascites, increased hematocrit, and prolonged sleeping times (Beauchamp et al. 1985). Acquired tolerance to acrolein in mice given repeated intraperitoneal injections suggests that an increased metabolism can partially explain the acquired tolerance (Warholm et al. 1984).

The largest number of studies of the toxicity of acrolein in animals was conducted by way of inhalation, probably because acrolein has an appreciable vapor pressure under ambient conditions and inhalation is the principal exposure for humans (Beauchamp et al. 1985). Because of their intolerance to sharp and offensive odor and to intense irritation of conjunctiva and the upper respiratory tract, humans have not suffered serious intoxication from acrolein. The strong lacrimatory effect of acrolein usually is a warning to occupational workers. Physiological perception of acrolein by humans begins at about 500 to 1,000 µg/L air with eye and nasal irritation; the irritating effects compel afflicted individuals to immediately leave the polluted area (Beauchamp et al. 1985). Laboratory animals died from inhalation of 8,000–11,000 µg/L after 4–6 h, mice from 875,000 µg/L after 1 min and rats from 660 µg/L after 24 days (Table 4). Animals dying from acute and subacute exposure to acrolein vapor had lung injury with hemorrhagic areas and edema (Albin 1962). Repeated

Table 4. Acrolein effects on selected mammals.

Organism, route of administration, dose, and other variables	Effect	References[a]
Cow, *Bos* sp.; drinking water route; lactating dairy cows given 60,000 µg acrolein/L for 24 h	No change in feed or water intake or milk production; acrolein residues in milk <500 µg/L	1
Dog, *Canis familiaris*; inhalation route		
220, 1,000 or 1,800 µg/L air (0.5, 2.3, or 4.1 mg/m^3); continuous exposure for 90 days	Low concentration group appeared normal and gained weight. At 1,000 µg/L, ocular and nasal discharges. At the high concentration, severe irritation evident plus nonspecific inflammation of brain, heart, lung, liver, and kidney; no deaths	2
400–600 µg/L air for 1–3 min	81–84% of acrolein retained; accumulations greater in upper respiratory tract than lower respiratory tract	3,4
700 or 3,700 µg/L air (1.6 or 8.4 mg/m^3); exposure for 8 h daily, 5 days weekly for 6 weeks	Low concentration group appeared normal and gained weight. High concentration group visibly affected with weight loss, excessive salivation, ocular discharges, labored breathing, and histopathology of lung, liver, and kidney; blood and serum chemistry normal	2
150,000 µg/L air (340 mg/m^3) for 30 min	LC50	3, 5, 6
Guinea pig, *Cavia* spp.; inhalation route		
200, 1,000 or 1,800 µg/L continuously for 90 days	The low concentration group appeared normal. At 1,000 µg/L, pulmonary inflammation and liver necrosis. At high concentration, all had nonspecific inflammation of brain, heart, lung, liver, and kidney	2
400–1,000 µg/L for 2 h	Decreased respiratory rate; effects reversed after exposure stopped	6,7
400–1,000 µg/L for as long as 12 h	Concentration-related increases in respiratory resistance together with prolonged and deepened respiratory cycles	3
700 or 3,700 µg/L; 8 h daily, 5 days weekly for 6 weeks	Low concentration group seemed normal. At high concentration, histopathology of lung, liver, and kidney	2
10,500 µg/L for 6 h	LC50	6
20,000 µg/L for 10 min	Bronchioconstriction	6
Cat, *Felis domesticus*; inhalation route		
650,000 µg/L air for 2.25 h	Died within 18 h	6
870,000 µg/L air for 2.5 h	Died during exposure	6
Human, *Homo sapiens*; inhalation route		
20 µg/L air	Threshold for affecting electrocortical activity	6
30–40 µg/L air	Odor threshold for the most acrolein-sensitive people	6

Table 4. *Continued.*

Organism, route of administration, dose, and other variables	Effect	References[a]
90–300 µg/L air	Increasing concentration and increasing exposure caused increasing eye blinking, irritation, and decreasing respiratory frequency	8
140–150 µg/L air for 2 min	Eye irritation in 30% of subjects	6
250 µg/L air for 5 min	Moderate irritation of sensory organs	3, 5
300 µg/L air for 10 min	Considerable acute irritation	8
300–500 µg/L air	Odor threshold for most people	3, 6
1,000 µg/L air for 1 min	Slight nasal irritation	3, 5
1,000 µg/L for 5 min	Moderate nasal irritation; intolerable eye irritation	3,5
1,800 µg/L air for 1 min	Slight eye irritation	3
5,500 µg/L air for 20 sec	Painful eye and nasal irritation	3, 5
21,800 µg/L air for 1 sec	Intolerable	3, 5
Syrian golden hamster, *Mesocricetus auratus*		
Gavage route; 1,000 µg/animal, equivalent to about 4,000 µg/kg BW	Fatal within a few hours	11, 12
Inhalation route		
400 or 1,400 µg/L air; exposure for 6 h daily, 5 days weekly for 13 weeks	No adverse effects at low concentration; nasal histopathology at high concentration	9
4,000 µg/L air (9.2 mg/m^3); 7 h daily, 5 days weekly for 52 weeks	No effect on survival; no indication of cancer. Abnormal behavior, growth retardation, increased lung weight, decreased liver weight, nasal histopathology	10
6,000 µg/L air (13.8 mg/m^3) for 4 h	Cytotoxic to airway cells	3
25,400 µg/L air for 4 h	LC50	6, 10
Mouse, *Mus* sp.		
Drinking water route; 24,000 µg/L for 18 months	Death	29
Inhalation route		
10 µg/L air continuously for 5 weeks	Some reduction in pulmonary compliance	4
1,000–2,000 µg/L (2.3–4.6 mg/m^3) air for 24 h	Decreased pulmonary ability to kill bacteria *Staphylococcus aureus* and *Proteus mirabilis*	3
1,700 µg/L air for 10 min	50% reduction in respiratory rate	6,14
3,000 or 6,000 µg/L air for 8 h	Concentration-dependent impairment of pulmonary antibacterial responses	15
6,000–15,000 µg/L air; 6 h daily, 5 days weekly for 6 weeks	Decreased body weight (6%) in all test groups, but not concentration-related	3
66,000 µg/L for 6 h	LC50, 24 h post-exposure	6
175,000 µg/L air for 10 min	LC50	3, 5, 6
875,000 µg/L air for 1 min	LC50	3, 5, 6
Intraperitoneal injection route		
4,000 µg/kg BW; single injection	Plasma total lactic dehydrogenase activity (LDH) increased 5 times, with peak after 10 h	16
4,000 µg/kg BW; multiple daily or weekly injections	Progressively less pronounced effect on LDH activity	16

Table 4. *Continued.*

Organism, route of administration, dose, and other variables	Effect	References[a]
7,000 µg/kg BW; single injection	LD50	16
12,000 µg/kg BW; preceded by daily injections of 4,000 µg/kg BW for 5 days	50% mortality	16
Oral route; 28,000 µg/kg BW	Acute oral LD50	3, 4, 5, 6
Rabbit, *Oryctolagus* sp.		
Dermal route; immersed up to necks for 60 min in water with 20,000 µg/L	No adverse effects	1
Drinking water route		
9,000 µg/L for 13 days	Miscarriages	29
36,000 µg/L for 13 days	Stomach ulcers	29
Inhalation route		
400 or 1,400 µg/L; 6 h daily, 5 days weekly for 13 weeks	No adverse effects at low concentration; some signs of distress at 1,400 µg/L	9
600 µg/L; 4 h daily for 30 days	No ocular effects	2
1,700–2,400 µg/L for 10 min; with or without 1,000 µg ozone/L	Acrolein alone had no effect on respiratory rate. Ozone-acrolein mixtures produced a marked decrease in respiratory rate	6
4,900 µg/L air; 6 h daily, 5 days weekly for 13 weeks	Ocular and nasal irritation, growth depression, respiratory tract histopathology	10
6,500–10,500 µg/L; exposure duration unknown	Emphysema, tracheobronchitis, some deaths	2
10,500 µg/L air for 6 h	LC50	6
Intravenous injection route; 3,000, 4,500 or 6,000 ug acrolein/kg BW on day 9 of gestation; killed on day 28 of gestation	Embryo resorption was significantly higher in 6,000 µg/kg group vs. controls, but was the same as controls in lower concentration groups	6
Percutaneous injection route		
164,000 µg/kg BW	LD50 for 20% acrolein in mineral spirits	3, 5
238,000 µg/kg BW	LD50 for 10% acrolein in mineral spirits	3, 5
335,000 µg/kg BW	LD50 for 20% acrolein in water	3, 5
562,000 µg/kg BW	LD50 for undiluted acrolein	3, 5
1,022,000 µg/kg BW	LD50 for 10% acrolein in water	3, 5
Domestic sheep, *Ovis aries*; inhalation route via cervical trachea; ewes, 3–4 years old; exposed to smoke containing high (but unknown) concentrations of acrolein for 20 min; killed 1–22 days after exposure	Within 24 h of exposure there was sloughing of total cervical tracheal epithelium and a 35% reduction in tracheal basal cells; trachea was normal 18–22 days after exposure	13
Baboon, *Papio anubis*; inhalation route. Juveniles exposed to air concentrations of 12,000–2,780,000 µg acrolein/L (272–63,100 mg/m^3) for 5 min, then tested for learned avoidance/escape response	Avoidance/escape response enhanced in all animals at all concentrations tested. The group exposed to 1,025,000 µg/L air died with respiratory complications within 24 h post-exposure. The group exposed to the highest concentration of 2,780,000 µg/L for 5 min died for 5 min died within 90 min postexposure with severe respiratory complications	17

Table 4. *Continued.*

Organism, route of administration, dose, and other variables	Effect	References[a]
Laboratory white rat, *Rattus* **sp.**		
Dermal route; exposure duration and dose unknown	Skin burns; severe ocular effects	18
Drinking water route		
5,000, 13,000, 32,000, 80,000 or 200,000 µg/L for 12 weeks	Water consumption in the 200,000 µg/L group was reduced by about 33% for the first 3 weeks; by week 12, all groups appeared normal and had apparently adapted to the odor and taste of acrolein	4
80,000 µg/L for 3 days	Some deaths	29
100,000 or 250,000 µg/L for 124 weeks	No increase in tumors over controls; no decrease in survival	11
100,000, 250,000 or 625,000 µg/L for 120 weeks	No significant decrease in survival when compared to controls. The 100,000 µg/L group had a 30% frequency of liver neoplasms and a 5% frequency of adrenal cortex neoplasms; however, no neoplasms were found in the 250,000 µg/L group. The 625,000 µg/L group had a 10% frequency of liver neoplasms vs. 25% in controls	12
200,000 µg/L for 90 days	No adverse effects	1
600,000, 1,200,000 or 1,800,000 µg/L for 60 days	Rats in the two high-concentration groups refused to drink and all died, apparently from dehydration. In the low-concentration group 20% died, but survivors were not dehydrated and had no tissue pathology	4
625,000 µg/L for 100 weeks	No decrease in survival; 20% of females developed adrenal cortical ademonas and 10% had neoplastic nodules in the adrenal cortex vs. 0% in controls	6
625,000 µg/L for 104 weeks	No decrease in survival. Increased frequency of adrenal cortex adenomas in females: 25% vs. 1.3% in controls	11
Inhalation route		
10 or 50 µg/L air for 1 min	Increased blood pressure and heart beat rate	19
10, 500, 1,000, or 2,400 µg/L air for 3 h	At 500 µg/L and higher, effects on respiratory mucosa included depletion of nonprotein sulfhydryl (NPSH) concentration and slight decrease in protein sulfhydryl (PSH) concentration. Effects on olfactory mucosa showed no changes in PSH at all test concentrations, but significant depletion of NPSH in the two high-concentration groups	20

Table 4. *Continued.*

Organism, route of administration, dose, and other variables	Effect	References[a]
100, 1,000, or 3,000 µg/L air, exposed 6 h daily, 5 days weekly for 3 weeks	No adverse effects in the two low-concentration groups. The high concentration group had depressed spleen weight and body weight and extensive nasal histopathology	14
150, 510, or 1,520 µg/L air; continuous exposure for 61 days	At low concentration, no respiratory tract lesions or deaths. At 510 µg/L, bronchial epithelium abnormalities but all survived. At high concentration, reduced survival; bronchopneumonia and bronchial abnormalities in survivors	6
220 or 660 µg/L air; exposed continuously for 60 days	No deaths at 220 µg/L; 70% died within 24 days at 660 µg/L	2
220, 1,000 or 1,800 µg/L air, exposed continuously for 90 days	The low concentration group appeared normal and gained weight. At 1,000 µg/L, liver necrosis and pulmonary hemorrhage. At 1,800 µg/L, all had nonspecific inflammation of brain, heart, lung, liver, and kidney	2
400 µg/L air; exposed 6 h daily, 5 days weekly for 13 weeks	Nasal histopathology	9
400, 1,400, or 4,000 µg/L air; exposed 6 h daily, 5 days weekly for 62 days	Some bronchial histopathology at 1,400 µg/L; some deaths among males at 4,000 µg/L	6
520 µg/L (1.2 mg/m^3); continuous exposure for 30 days	Decreased growth, altered liver enzyme activity	3
550 ug/L air; continuous exposure for up to 77 days	Upper respiratory irritation, reduced resistance to infection by *Salmonella*, and increased pulmonary macrophages; all effects disappeared by day 63	6
700 or 3,700 µg/L air; exposed 8 h daily, 5 days weekly for 6 weeks	No adverse effects noted at low concentration. At 3,700 µg/L, histopathology of lung, liver, and kidney	2
2,000 µg/L air for 40 h	Increased hepatic alkaline phosphatase activity; increased liver and adrenal weight	3
2,500–5,000 µg/L air for 1 min	Cardioinhibitory effect that was reversed within 10 sec after inhalation of acrolein ceased	19
4,900 µg/L air; exposed 6 h daily, 5 days weekly for 13 weeks	50% mortality during first 4 weeks with no deaths thereafter. Survivors had depressed growth and respiratory tract histopathology	9
6,000–8,888 µg/L air; exposed 6 h daily, 5 days weekly for 3 weeks	Most died within 5 exposure days	14
8,000–8,300 µg/L air for 4 h	LC50 within 14 days; death due to lung injury	5, 6, 21

Table 4. *Continued.*

Organism, route of administration, dose, and other variables	Effect	References[a]
26,000 µg/L air for 1 h	LC50	21
43,500–304,000 µg/L air for 30 min	Respiratory distress; nasal and ocular irritation; some deaths in 4–5 days; pulmonary edema; bronchial degeneration; excess blood in heart, liver, and kidney	2, 6
131,000 µg/L air for 30 min	50% dead in 3 weeks	6
283,000 µg/L air; daily 10-min exposures for 6 months	No deaths; some bronchial pathology	6
326,000 µg/L air; daily 10-min exposures for 6 months	50% dead; tracheobronchial pathology	6
435,000 µg/L air; daily 10-min exposures for 6 months	All dead; severe histopathology of respiratory tract	6
5,000,000–10,000,000 µg/L air for 5 min	Rats on a motor-driven exercise wheel were incapacitated within 5–7 min and died shortly thereafter	17
Intraamniotic injection route		
Embryos given 0.1, 1, 10, or 100 µg of acrolein on day 13 of gestation; examined on day 20 of gestation	98–100% dead at 10 and 100 µg; 85% of live fetuses receiving 1 µg were malformed (edema, hydrocephaly, cleft palate, defects of limbs and tail); no teratogenic effects at 0.1 µg	6
Intraperitoneal injection route		
1,000 µg/kg BW, single injection	Peritonitis	22
1,000 µg/kg BW daily for at least 5 days	Lethal	22
2,000 µg/kg BW twice a week for 6 weeks followed by uracil as 3% of the diet for 20 weeks, then control diet for 6 weeks	Acrolein followed by uracil produced a 60% incidence of papilloma in urinary bladder in treated group (acrolein plus uracil) vs. 27% in water controls (uracil only). No tumors in either group	22
2,500 µg/kg BW daily	All dead after second dose	3
3,360 µg/kg BW; single injection; tissues analyzed after 24 h	Most (89%) of the acrolein recovered was in the acid-soluble fraction of the liver, 3% in the liver lipids, and minor amounts (0.4–1.7%) in liver proteins and RNA and DNA fractions	3
Intravenous injection route		
50–500 µg/kg BW to spontaneously hypersensitive rats	At 50–200 µg/kg BW, blood pressure increased; at 300–500 µg/kg BW, blood pressure decreased	23
250–1,000 µg/kg BW	Increased blood pressure within 5 sec which peaked at 20–30 sec and lasted about 1 min	19
850 or 1,700 µg/kg BW	Liver necrosis	3
10,000 µg/kg BW	Cardioinhibitory effects	19

Table 4. *Continued.*

Organism, route of administration, dose, and other variables	Effect	References[a]
In vitro studies		
Cultured embryos		
4,500 µg/L serum medium	Growth retardation; 50% malformation frequency among survivors	24, 25
6,700 µg/L serum medium	Mortality of 64%; all surviving embryos malformed	24, 25
7,800–9,000 µg/L serum medium	All dead	24, 25
160 µg/L serum-free medium	50% frequency of malformations in brain, facial area, and heart	25
300–1,100 µg/L serum-free medium	50%–100% lethal	25
Cultured myocytes and fibroblasts from neonatal heart		
600 µg/L culture medium for 4 h	Myocyte ATP levels reduced	26
2,800 µg/L culture medium for 4 h	Irreversible cell lysis and ciliostasis	26
Isolated liver fractions		
1,700 µg/L medium	Mitochondrial aldehyde dehydrogenase (ALDH) activity inhibited 91%; cytosolic ALDH activity inhibited 33%	27
2,700 µg/L medium; 5 sec preincubation in aldehyde substrate	Inhibition of mitochondrial and cytosolic ALDH	27
Oral route		
Daily gavage of 50, 500, or 2,500 µg/kg BW for 102 weeks	Dose-related mortality in males during first year and in females during entire study; significant lethality in the 500 and 2,500 µg/kg groups. No increased incidence of microscopic neoplastic or nonneoplastic lesions in treated rats; decreased creatinine phosphokinase levels in treated rats	28
Two treatments of 4,000–10,000 µg/kg BW (estimated), 2–3 days apart; total dose of 8,000–20,000 µg/kg BW	All died shortly after the second dose	12
5,000 µg/kg BW daily for 9 days via stomach intubation	No deaths	3
10,000 µg/kg BW, single stomach intubation	Fatal	3
25,000 µg/kg BW, single gastric dose	LD50 within 48 h	22
42,000–46,000 µg/kg BW, single dose	LD50 within 14 days	3, 4, 5, 6, 18,22
Squirrel monkey, *Saimiri sciurea*; inhalation route		
220, 1,000, or 1,800 µg/L air;	Low concentration group appeared	2

Table 4. *Continued.*

Organism, route of administration, dose, and other variables	Effect	References[a]
continuous exposure for 90 days	normal and gained weight; 1,000 µg/L monkeys were visibly affected with ocular and nasal discharges. No deaths at 1,800 µg/L, but excessive salivation, ocular discharges, and hyperplasia of trachea	
700 or 3,700 µg/L air; 8 h daily, 5 days weekly for 6 weeks	Low concentration group appeared normal. High dose group had weight loss; histopathology of lung, liver, and kidney; 22% mortality (2 of 9 died on days 6 and 9 of exposure) excessive salivation, and frequent blinking	2

[a] 1, Ferguson et al. 1961; 2, Lyon et al. 1970; 3, EPA 1980; 4, NRC 1977; 5, Albin 1962; 6, Beauchamp et al. 1985; 7, Leikauf et al. 1989; 8, Weber-Tschopp et al. 1977; 9, Feron et al. 1978; 10, Feron and Kruysse 1977; 11, Lijinsky and Reuber 1987; 12, Lijinsky 1988; 13, Barrow et al. 1992; 14, Leach et al. 1987; 15 Astry and Jakab 1983; 16, Warholm et al. 1984; 17, Kaplan 1987; 18, Sine 1991; 19, Egle and Hudgins 1974; 20, Heck et al. 1986; 21, Ballantyne et al. 1989; 22, Cohen et al. 1992; 23, Green and Egle 1983; 24, Slott and Hales 1987; 25, Slott and Hales 1986; 26, Toraason et al. 1989; 27, Mitchell and Petersen 1988; 28, Parent et al. 1992; 29, ATSDR 1990.

exposures of hamsters, rats, and rabbits to high sublethal concentrations of acrolein caused ocular and nasal irritation, growth depression, and respiratory tract histopathology in all species (Feron and Kruysse 1977; Table 4). However, repeated exposures to low, tolerated concentrations of acrolein did not produce toxicological effects (Albin 1962), suggesting that acrolein effects are not cumulative and that minimal damage is quickly repaired.

Inhaled acrolein—in µg acrolein/L air—had sublethal effects at 10–50 for 1 min on rats (increased blood pressure and heart rate); at 10 for 5 weeks on mice (reduction in pulmonary compliance); at 140–150 for 2 min on humans (eye irritation in 30%); at 300–500 on humans (odor threshold); at 300 for 10 min on humans (acute irritation); at 400 for 13 weeks on rats (nasal histopathology); at 400–600 for 1–3 min on dogs (accumulations in upper respiratory tract); and at 1,000 for 90 days on dogs, monkeys, and guinea pigs (ocular and nasal discharges; Table 4). Sublethal effects of inhaled acrolein in representative small laboratory mammals were greatest on the upper respiratory tract and bronchial airways and included edema, ciliastasis, inflammation, degenerative loss of epithelia, altered ventilatory function, and bronchoconstriction (Feron and Kruysse 1977; Feron et al. 1978; EPA 1980; Astry and Jakab 1983; Beauchamp et al. 1985; Barkin et al. 1986; Leach et al. 1987; Leikauf et al. 1989; Table 4). Typical signs of toxicity from inhaled acrolein in small mammals include ocular and nasal irritation; growth depression; shortness of breath; lesions in the urinary tract, respiratory tract, trachea, and nasal passages; laryngeal edema; reduced resistance to bacterial infection; enlarged liver and heart; elevated blood pressure and heart rate; altered enzyme activities; and protein synthesis inhibition (EPA 1980; Beauchamp et al. 1985; Leach et al. 1987; Table 4). Signs of inhaled acrolein toxicity varied significantly with dose and species. For example, acrolein toxicity in rats at environmental concentrations was confined to local pathologic nasal changes, including metaplastic, hyperplastic, and dysplastic changes in the mucous, respiratory, and olfactory epithelium of the nasal cavity (Leach et al. 1987). Some inhaled toxicants, including acrolein, can prolong bacterial viability in the lung and thus enhance severeness of the disease. Mice convalescing from viral pneumonia became severely deficient in antibacterial defenses when exposed to acrolein (Astry and Jakab 1983). But acrolein-treated mice subjected to 100 µg/L air (5 consecutive daily 3-h exposures) were not significantly sensitive to pulmonary bacteria *Klebsiella pneumoniae* or *Streptococcus zooepidemicus* (Aranyi et al. 1986).

Acrolein may be a carcinogen, cocarcinogen, or tumor initiator. As an aldehyde with strong affinity to sulfhydryl groups, acrolein is theoretically

expected to remove free tissue thiols—compounds that protect bronchial epithelia against attack by carcinogens (Feron and Kruysse 1977; Feron et al. 1978). Carcinogenicity from inhalation of acrolein has not been reported (Lijinsky and Reuber 1987), and acrolein was not an evident cofactor in studies of respiratory-tract carcinogenesis with hamsters (*Cricetus* spp.) exposed to benzo(a)pyrene or diethylnitrosamine (Feron and Kruysse 1977). Moreover, long-term studies with rodents given acrolein by gavage did not increase incidences of neoplastic or nonneoplastic lesions (Parent et al. 1992). Other studies, however, suggest that acrolein is carcinogenic. Compounds closely related to acrolein are carcinogenic to rodents and humans and include acrylonitrile (vinyl cyanide) and vinyl acetate (Lijinsky 1988). Glycidaldehyde—an acrolein intermediate metabolite—is classified as an animal carcinogen by The International Agency for Research on Cancer; however, no convincing data are available on the carcinogenic potential of acrylic acid and other acrolein metabolites (Beauchamp et al. 1985). Acrolein at least partially can account for the initiating activity of cyclophosphamide carcinogenesis (Cohen et al. 1992). Cyclophosphamide and its analogs are a group of chemotherapeutic and immunosuppressive drugs; toxic side effects of this drug group are attributed to its metabolites, especially acrolein (Cohen et al. 1992). Acrolein is a suspected carcinogen because of its 2,3-epoxy metabolite and its weak mutagenic activity in the *Salmonella* screen (Leach et al. 1987). Acrolein may be a weak carcinogen, as judged by the increased frequency of adrenal adenomas in female rats after exposure for 2 years to drinking water with 625,000 µg acrolein/L (Lijinsky and Reuber 1987). Acrolein has cancer-initiating activity in the rat urinary bladder, but studies with N-[4-(5-nitro-2-furyl)-2 thiazoyl] formamide precluded evaluation of acrolein as promoting a complete carcinogenic activity from low rodent survival (Cohen et al. 1992). Additional studies seem needed to evaluate the carcinogenic potential of acrolein.

After intraamniotic injection, acrolein is teratogenic to rats in vivo but not in vitro. When administered intraamniotically to the whole embryo culture system of the rat on day 13 of gestation, acrolein caused edema, hydrocephaly, open eyes, cleft palate, abnormal umbilical cord, and defects of the limbs and face (Slott and Hales 1986). Beauchamp et al. (1985) suggest that acrolein-associated teratogenicity is caused by acrylic acid, an acrolein metabolite. Acrylic acid injected into amniotic fluid of rats on day 13 of gestation produced a dose-dependent increase in the percentage of fetuses with skeletal and other abnormalities (Beauchamp et al. 1985).

Acrolein can react synergistically, additively, or antagonistically with other chemicals (Beauchamp et al. 1985). Rat embryos were protected by glutathione against acrolein-induced mortality, growth retardation, and developmental abnormalities—provided that glutathione was concurrently present with acrolein. When rat embryos were cultured in the presence of acrolein for 2 h prior to glutathione exposure, there was no protection against acrolein-induced embryolethality, teratogenicity, and growth retardation (Slott and Hales 1987). Acrolein effects—including altered liver-enzyme activity in rats—were reduced by pretreatment of animals with chemicals that inhibited protein synthesis (NRC 1977). Exposure to acrolein is sometimes accompanied by exposure to formaldehyde and other short-chain saturated aliphatic aldehydes, which in combination cause allergic contact dermatitis (Susten and Breitenstein 1990). A 40-mL puff of cigarette smoke contains 8.2 µg of acrolein and 4.1 µg of formaldehyde; irritation, ciliastasis, and pathologic changes of the respiratory tract from both compounds have been widely studied (Egle and Hudgins 1974). The toxicities of acrolein and formaldehyde seem similar; both exert their principal effects in the nasal passages (Leach et al. 1987). Acrolein in combination with formaldehyde was synergistic in reducing respiratory rates in mice; however, mixtures of sulfur dioxide and acrolein were antagonistic (Beauchamp et al. 1985). Formaldehyde pretreatment (15,000 µg/L, 6 h daily for 9 days) of rats protects against respiratory-rate depression by acrolein. Rats pretreated with formaldehyde had a 50% respiratory-rate depression at 29,600 µg acrolein/L versus 6,000 µg/L from acrolein alone (Babiuk et al. 1985), suggesting cross tolerance. Effects of interaction of acrolein with other toxicants are not comparable between rodents and humans. In rodents, the presence of irritant gases in smoke—such as acrolein—may delay the effects of other toxicants. In humans, however, the inhalation of acrolein and other irritant gases may cause a hypoxemic effect that can enhance the effects of hypoxia-producing gases (Kaplan 1987).

Some chemicals normally contain acrolein as a metabolite or impurity. For example, allylamine toxicity to the rat cardiovascular system is be-

lieved to involve metabolism of allylamine to the highly reactive acrolein (Toraason et al. 1989). Certain mercapturic acids can be used as biological markers of exposure for chemicals that are metabolized to acrolein and excreted as mercapturic acid in the urine (Sanduja et al. 1989). In one case, rats given 13,000 µg acrolein/kg BW by gavage excreted 79% of the acrolein and 3-hydroxypropylmercapturic acid (3-OHPrMCA) in urine within 24 h. These data suggest that 3-OHPrMCA can be used as a marker of exposure to allylic and other compounds that lead to the formation of acrolein (Sanduja et al. 1989). The common industrial chemical MDP (2-methoxy-3,4-dihydro-2PH-pyran) is frequently contaminated with acrolein during its synthesis; MDP causes severe irritancy and death of rats from accumulation of acrolein vapor (Ballantyne et al. 1989). Sparging acrolein-contaminated MDP with nitrogen gas before atmospheric release significantly reduced or abolished lethal toxicity to rats (Ballantyne et al. 1989).

Recommendations

Agricultural crops can usually tolerate as much as 15,000 µg of acrolein/L of irrigation water; however, aquatic invertebrates and fish die in acute exposures to 55–68 µg/L or in chronic exposures to greater than 21 µg/L (Table 5). Those who use acrolein to control submerged aquatic macrophytes are strongly advised that acrolein treatment at recommended application concentrations also eliminates nontarget fish and aquatic invertebrates. No acrolein criteria are now available or promulgated by regulatory agencies for the protection of avian and terrestrial wildlife; this seems to be a high-priority research need. Beauchamp et al. (1985) recommend additional research in several areas: long-term effects of acrolein inhalation on carcinogenicity and respiratory histology with rodent models; biochemical mechanisms of acrolein toxicity; genotoxic potential with chromosome breakage and exchange systems; acute and chronic toxicity from interaction effects of acrolein with other gases; and fate of accumulated acrolein in animals.

The human threshold concentration of acrolein in the United States for an 8-h workday and 40-h workweek is 110 µg/L (0.25 mg/m^3) air; the short-term exposure limit is 350 µg/L (0.8 mg/m^3) air and is predicated on continuous exposure of workers for short intervals (Table 5; Beauchamp et al. 1985). Humans can tolerate a total daily intake of 47.8 µg of acrolein, equivalent to 0.68 µg/kg BW by a 70-kg individual (Table 5).

For handling acrolein, gloves, vapor-proof goggles or a full-face mask, and other protective clothing are mandatory (Albin 1962; Beauchamp et al. 1985; NIOSH 1990). Acrolein spills should be neutralized with 10% sodium bisulfite solutions (Albin 1962). Air packs or fresh-air breathing masks, safety showers, and eye baths should be available wherever acrolein is handled (Beauchamp et al. 1985). Purging confined areas with nitrogen is recommended prior to entering a suspected acrolein-contaminated enclosure. The eyes are particularly susceptible to liquid acrolein and, if exposed, should receive prompt treatment, although severe residual injury is probable regardless of treatment; dilute solutions of acrolein may also cause residual eye injury. Acrolein represents a serious fire hazard because of its high flammability and potential for vapors to form explosive mixtures with air. Flame-proof electrical equipment and proper grounding is required to prevent acrolein ignition. Individuals exposed to acrolein

Table 5. Proposed acrolein criteria for the protection of living resources and human health.

Resource, criterion, and other variables	Concentration	Reference[a]
Agricultural Crops		
Irrigation water, tolerated level	<15,000 µg/L	1
Aquatic life		
Freshwater organisms		
Sensitive species, tolerated level		
Acute exposures	<68 µg/L	2
Chronic exposures	<21 µg/L	2
Rainbow trout, safe level	20 µg/L for <48 h or 200 µg/L for <4.8 h	3

Table 5. *Continued.*

Resource, criterion, and other variables	Concentration	Reference[a]
Marine organisms; acute exposures, tolerated level	<55 µg/L	2
Laboratory white rat		
Air		
Maximum daily average	<13 µg/L (<0.03 mg/m^3)	7
Maximum daily	<44 µg/L (<0.1 mg/m^3)	7
Human health		
Air		
Maximum allowable emission concentration in populated areas of former Soviet Union	132 µg/L (0.3 mg/m^3)	4
No observable effect level	<22 µg/L (<0.05 mg/m^3)	4
90-day confined space (i.e., submarines) guideline	22 µg/L (0.05 mg/m^3)	5
Odor threshold	<44 µg/L (<0.1 mg/m^3)	4
Maximum acceptable concentration in room air of former Soviet Union	44 µg/L (0.1 mg/m^3)	2,4
Irritation threshold mg/m^3)	44–88 µg/L (0.1–0.2 mg/m^3)	4
Occupational exposure standard (8 h daily, 40 h work week) in United States; not to exceed in most European countries, Australia, and Japan	100–110 µg/L (0.25 mg/m^3)	2, 4, 5, 6, 8
Occupational exposure standard in Hungary and former Soviet Union	308 µg/L (0.7 mg/m^3)	4
Maximum 15-min exposure limit in USA workplace	300–352 µg/L (0.8 mg/m^3)	4, 8
Ceiling standard for occupational exposure in the former Czechoslovakia	440 µg/L (1.0 mg/m^3)	4
Acceptable ambient air concentrations		
New York	0.83 µg/m^3 for 1 year	9
Florida	2.5 µg/m^3 for 8 hr	9
North Dakota	8.0 µg/m^3 for 1 hr	9
North Carolina	80 µg/m^3 for 15 min	9
Diet		
Water plus consumption of contaminated aquatic organisms from that water body	<320 µg/L medium	2
Consumption of contaminated aquatic organisms alone	<780 µg/L medium	2
Food packaging materials; food starch	<0.6%	2
Total daily intake	<47.8 µg = <0.68 µg/kg body weight daily for a 70-kg person	2

[a] 1, Ferguson et al. 1961; 2, EPA 1980; 3, Bartley and Hattrup 1975; 4, Beauchamp et al. 1985; 5, Lyon et al. 1970; 6, Leach et al. 1987; 7, NRC 1977; 8, NIOSH 1990; 9, ATSDR 1990.

by inhalation should be removed from the area and given oxygen; subsequent treatment by physicians of pulmonary inflammation with corticosteroids and hydroxocobalamin is recommended even if there are no symptoms (Beauchamp et al. 1985) because adverse effects from acrolein exposure may not become apparent until 4–24 h after exposure (Albin 1962). Oxygen therapy should be continued and analgesics given for relief of other symptoms as necessary (Beauchamp et al. 1985). There are many synthetic and natural sources of acrolein; however, special precautions are recommended when acrolein occurs as a contaminant in the synthesis of widely used chemicals such as 2-methyoxy-3,4-dihydro-2H pyran (Ballantyne et al. 1989).

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